

REMARKS

Claims 1, 2, 4, 8, 9, 11 and 13-17 are pending in this application. No new matter is added.

Rejection under 35 U.S.C. §103

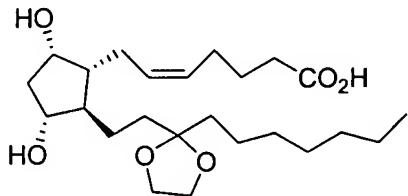
Claims 1, 2, 4, 7, 8, 9 and 11 are rejected under 35 U.S.C. §103, as being unpatentable over U.S. Patent 5,853,703 to Cerami (“Cerami”) in view EP 0 458 589 A1 to Kabushiki (“Kabushiki”). The Examiner states that while Kabushiki merely teaches a combination of prostaglandin and a cholinergic agent for lowering ocular pressure, this does not negate the fact that Kabushiki discloses known, “commercialized” cholinergic agents for treating glaucoma such as pilocarpine. Thus, since Kabushiki discloses that cholinergic agents when combined with prostaglandins are synergistically effective at lowering ocular pressure, one of ordinary skill in the art, absent evidence to the contrary, would reasonably expect cholinergic agents when combined with the thiazolium compounds of Cerami to effectively reduce ocular hypertension suffered in the patients in Cerami. *See*, Office Action at page 3.

Applicants submit that the Examiner’s assertion is incorrect and that one of ordinary skill in the art reading Kabushiki would not reasonably expect cholinergic agents, when combined with the thiazolium compounds of Cerami, to effectively reduce ocular hypertension.

Kabushiki merely discloses the combination of a cholinergic agent (pilocarpine) and a specific prostaglandin compound (13,14-dihydro-15-ketoprostaglandin) to treat ocular hypertension. Based on the Examiner’s reasoning *supra*, one of ordinary skill in the art would reasonably expect that the combination of a cholinergic agent (pilocarpine) with any prostaglandin would have the similar synergistic effects at lowering ocular pressure as the combination of pilocarpine and 13,14-dihydro-15-ketoprostaglandin. This is not the case.

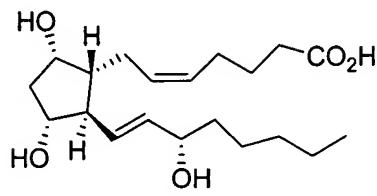
Kabushiki teaches that when a cholinergic agent, such as pilocarpine, is combined with other prostaglandins, such as PGF₂α (e.g., not 13,14-dihydro-15-ketoprostaglandin, the subject of the Kabushiki invention), the ocular pressure lowering activity of PGF₂α is inhibited by the cholinergic agent. *See*, Kabushiki page 2, lines 29-30. The skilled artisan reading Kabushiki would readily recognize that the art of combining any prostaglandin with any cholinergic agent is unpredictable: while one specific prostaglandin compound (13,14-dihydro-15-ketoprostaglandin) treats ocular hypertension in combination with a cholinergic agent, other compounds in the prostaglandin family with very similar structures and which are thought to

posses similar biological function, are unable to lower ocular pressure and treat ocular hypertension (**Emphasis Added**). Compare:



13,14-dihydro-15-ketoprostaglandin

with



PGF2a

Therefore, although all prostaglandins are similar in structure (all contain 20 carbon atoms, including a non-planar 5-membered aliphatic ring), all prostaglandins do not have similar functional activity when combined with a cholinergic agent, such as pilocarpine.

Since prostaglandins and thiazolum compounds (aromatic 5-membered rings) are structurally and functionally distinct, and because the teachings of Kabushiki show that the combination of any prostaglandins with any cholinergic agents is not reasonably expected to be effective in treating ocular hypertension, Applicants submit that the skilled artisan would have no reasonable expectation of success combining the methods of using the thiazolum compounds of Cerami with the prostaglandin/cholinergic compounds used in the methods of Kabushiki to reach the present invention.

Applicants respectfully request this rejection should be withdrawn.

CONCLUSION

On the basis of the foregoing amendment and remarks, Applicants respectfully submit that the pending claims are in condition for allowance and a Notice of Allowance for the pending claims is respectfully requested. If there are any questions regarding this application that can be handled in a phone conference with Applicants' Attorneys, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,


Ivor R. Elrifi, Reg. No. 39,529
Attorney for Applicant
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No.: 30623

Dated: March 8, 2005